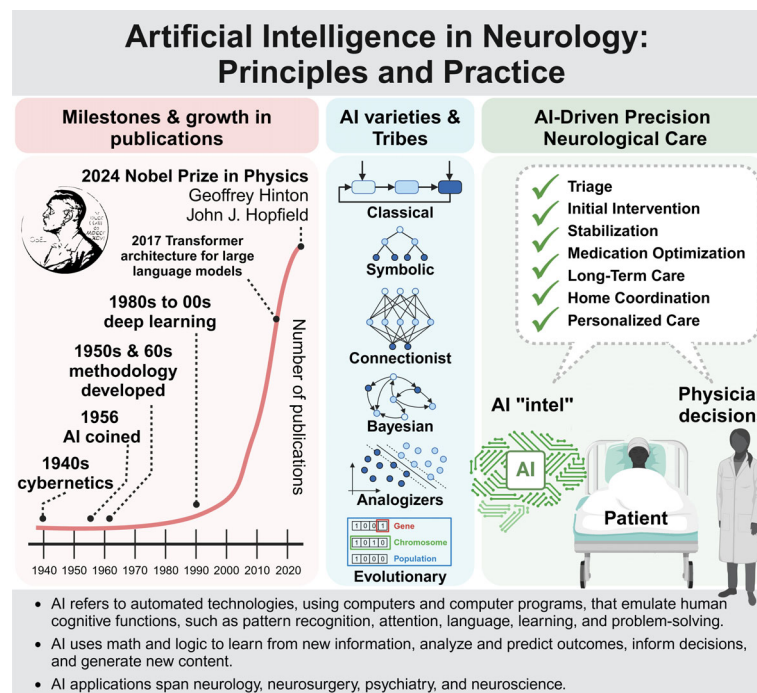


AI in Neurology: Everything, Everywhere, All at Once Part 1: Principles and Practice

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Artificial intelligence (AI) is rapidly transforming healthcare, yet it often remains opaque to clinicians, scientists, and patients alike. This review, part 1 of a 3-part series, provides neurologists and neuroscientists with a foundational understanding of AI's key concepts, terminology, and applications. We begin by tracing AI's origins in mathematics, human logic, and brain-inspired neural networks to establish a context for its development. The review highlights AI's growing role in neurological diagnostics and treatment, emphasizing machine learning applications, such as computer vision, brain-machine interfaces, and precision care. By mapping the evolution of AI tools and linking them to neuroscience and human reasoning, we illustrate how AI is reshaping neurological practice and research. We end the review with an overview of model selection

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in AI and a case scenario illustrating how AI may drive precision neurological care. Part 1 sets the stage for part 2, which will focus on practical applications of AI in real-world scenarios where humans and AI collaborate as joint cognitive systems. Part 3 will examine AI's integration with extensive healthcare and neurology networks, innovative clinical trials, and massive datasets, expanding our vision of AI's global impact on neurology, healthcare systems, and society.

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Data are the lifeblood of modern neurology practice, knowledge, and learning and necessary to advance mind and brain health, care, and cures for all peoples and communities. These data are present everywhere within the “exposome,” the sum of all real-world chemical, physical, biological, behavioral, and social factors that influence human health over the lifespan.^{1,2} The exposome, in turn, interacts with genetics and various “omics” biomarker data, shaping individual susceptibility, resilience, and phenotypes in neurological health and disease throughout life.

Sensors ubiquitously embedded in devices, vehicles, buildings, homes, appliances, clothing, people, and urban infrastructures—collectively part of the “internet of things”—continuously monitor performance, behavior, and physiology within varying social and environmental contexts. These real-world “digital biomarker” data can be combined with self-reports and ecological momentary assessments (experience sampling) on cognitive, affective, and conative status (related to volition and goal-directed behavior), providing unprecedented longitudinal observations of the “brain in the wild.”³

New artificial intelligence (AI) and machine learning (ML) strategies and techniques can classify, aggregate, reduce, and analyze these torrents of health informatics data to drive medical discovery.⁴ AI overcomes the “curse of dimensionality”⁵ in highly complex neurological data sets, which are often not addressed by conventional biostatistical and epidemiological methods. This review on AI in neurology outlines current applications as well as applications on the horizon, underscoring priority issues for further development. There is no universal consensus on definitions of the terms used here, nor in how topics relate together conceptually and historically. No one can claim expertise across the “big bang” expanse of AI, and must achieve proficiencies—native, fluent, or conversational—in facets most pertinent to their professional and daily lives, acting locally while thinking globally.

Part 1 covers AI definitions, milestones, varieties, logic, biases, model selection, and various AI types, such as ML, deep learning, deep neural networks (DNNs), and generative AI (Fig 1). Part 1 will also cover the proliferation of AI applications in neurology and neuroscience, including computer vision, human brain-machine interfaces, and disease prediction. Part

2 will examine real-world applications and the development of AI-enabled social and emotional robots and their looming sentience and the social, legal, and ethical foundations of AI, including concerns on privacy and protection of vast neurological data. The introduction of new tools generates deep questions on large-scale integration of AI into many facets of society, paving the way for discussion on sociotechnical systems in part 3 (Fig 1). A glossary spans all sections.

As we shall see, AI, combined with modern organizational principles and practices,⁶ ever-increasing computing power, analytic insights, and systems

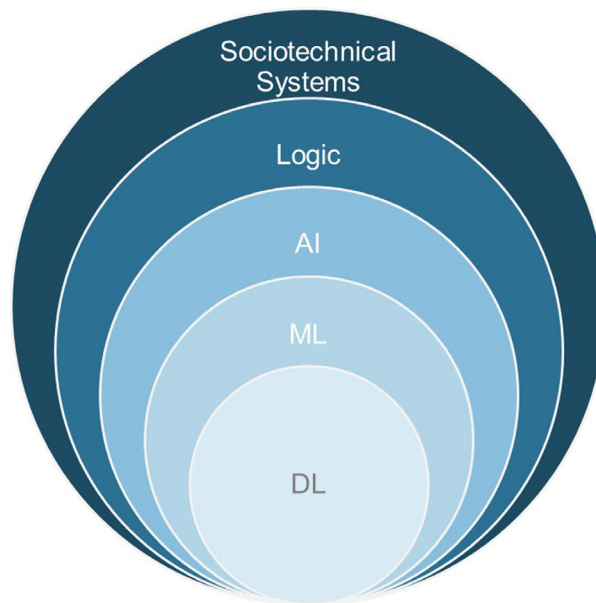


FIGURE 1: Hierarchical relationships between logic, artificial intelligence (AI), machine learning (ML), and deep learning (DL) within sociotechnical systems for healthcare. Logic forms the foundation for reasoning and systematic thinking. AI leverages logical structures for intelligent machine behavior. ML involves algorithms that generate models, which improve through training. DL, a specialized ML area, focuses on multi-layered neural networks, including convolutional neural networks, generative adversarial networks, and large language models. Robotics relies on AI for perception, planning, and decision-making, and on ML for adaptive functions. Robotics also involves mechanical engineering, sensors, and control systems beyond AI's scope. Standard statistics, fundamental to neuroscience and other fields, fit primarily within the “Logic” oval, extends into “AI,” and is deeply embedded in ML for training and evaluation. Sociotechnical systems represent the broadest context, encompassing human, organizational, and technological elements bound by AI and operated by humans. [Color figure can be viewed at www.annalsofneurology.org]

science, are key to neurological advances, which seem to affect everything we do in neurology and healthcare, everywhere, all at once.

What Is AI?

AI refers to the ability of automated technologies, using computers and computer programs, to emulate human cognitive functions, such as learning and problem-solving. AI technologies use math and logic to learn from new information, analyze and predict outcomes from large datasets, make decisions from incomplete data using probabilistic models, and generate new content and synthetic data. AI spans a variety of application areas and tools, including ML, robotics, computer vision, natural language processing (NLP), knowledge representation, reasoning and problem solving, and expert systems that mimic human thinking in specific domains.

ML, an AI subset, develops algorithms that help computers learn from experience to make decisions. Algorithms (named after the 9th century mathematician Al-Khwārizmī⁷) are sets of rules or instructions for processing data inputs to generate outputs. ML algorithms manifest as computer programs that create models by learning from data, their quality and integrity largely dependent on the quality of the training data.

A model is a mathematical representation that recognizes and interprets patterns in data. AI uses models to derive insights, often represented as probabilities. Probabilistic approaches include Bayesian networks (graphical models), hidden Markov models (statistical models), and Markov Chain Monte Carlo methods (algorithms that sample from probability distributions).⁸ Mathematical models generally represent processes in various fields, for example, Newton's laws describe physical phenomena, financial models predict market behaviors, and the susceptible, exposed, infected, recovered/removed model in epidemiology represents the spread of diseases. In AI, the same algorithm can be adapted to different models depending on the data it is trained on, demonstrating the versatility of these computational tools.

Therefore, algorithms are the procedures for processing data, whereas models are the resulting structures that encapsulate the learned knowledge from the data. Algorithms can code a Fibonacci sequence, control traffic lights, or alphabetize words in a dictionary. Models, fit by computer programs, represent a part of the world mathematically.

One real-world example of AI in neurology is the use of ML algorithms to analyze medical imaging data, such as magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) scans, identifying patterns and anomalies. These algorithms train models by fitting them to vast amounts of imaging data,

optimizing their ability to generalize and detect clinically relevant features. Well-fitted models enhance diagnostic accuracy, enabling AI systems to provide insights that human clinicians might miss. This leads to earlier detection and more accurate diagnoses of neurological conditions, such as Alzheimer's disease, stroke, and brain tumors. Throughout this review, we will explore how AI applications in neurology continue to refine patient care.

AI Milestones

John McCarthy coined the term AI at the 1956 Dartmouth Conference, seemingly marking the field's debut. However, AI is rooted in earlier innovations dating back centuries originating from deeper understandings of logic, causal reasoning, mathematics, and statistics (Table 1). Nineteenth century mathematical innovations, along with early 20th century hypothesis testing and statistical methods, set the stage for more complex AI systems.

In the 1940s, Norbert Wiener¹⁶ introduced cybernetics, a field crucial for understanding control systems and communication in animals and machines, significantly influencing early AI development. McCulloch and Pitts advanced early models of biologically inspired neural networks, laying foundational concepts for future AI.¹⁷ The 1950s and 1960s witnessed the development of essential AI methodologies, such as search algorithms, logic programming, and optimization techniques.

The recent AI revolution launched with the emergence of deep learning, which Hinton, LeCun, Bengio, and others had been exploring for some time, from the 1980s through the early 2000s (see "Neural Networks: History and Underpinnings" section).^{35,45} A deep learning model significantly outperformed other types of models, primarily support vector machines, at the 2011 to 2012 ImageNet competition, compelling researchers to reconsider neural networks as serious contenders for building AI systems following a period of skepticism.⁴⁶

Discriminative deep learning models, such as convolutional neural networks (CNNs) and recurrent neural networks (RNNs) excel at image classification, object detection, and language translation, with great success, for instance, in medical document and image analysis.^{47–50} Generative deep learning models, such as generative adversarial networks (GANs) and variational autoencoders (VAEs), learn from the underlying distribution of input data and rapidly gained popularity for their impressive outputs, like realistic images, music, and text.^{51,52}

"*Attention is All You Need*" by Vaswani et al³⁸ introduced transformers neural networks, which leverage a mechanism called self-attention to process entire input sequences in parallel, unlike previous models that processed data

TABLE 1. AI Milestones

Epoch/ decade	Key contributions and developments
Early 19th century	Legendre ⁹ and Gauss ¹⁰ introduced regression analysis for astronomical data, a foundational method for understanding relationships between variables spread across scientific disciplines. Cauchy ¹¹ introduced the method of steepest descent (gradient descent), foundational to optimizing ML algorithms.
Mid-19th century	Boole ¹² published “ <i>An Investigation of the Laws of Thought</i> ,” introducing Boolean algebra, fundamental to the development of digital logic and computer science. Lovelace ¹³ created the first algorithm intended for a machine (the Analytical Engine), contributing to early conceptualization of computer science and programming.
Early 20th century	Key advances in statistical methods with hypothesis testing and “Student’s” <i>t</i> test, ¹⁴ Fisher ¹⁵ expanded with the introduction of ANOVA.
1940s	Emergence of cybernetics by Wiener ¹⁶ ; McCulloch and Pitts ¹⁷ advanced early models of neural networks; Hebb synapse ¹⁸ of “neurons that fire together wire together.”
1950s	McCarthy ¹⁹ coined the term AI in 1956; Munro ²⁰ advanced gradient descent; Rosenblatt (1958) developed the perceptron. ²¹
1960s	Traditional computer programming methods and early AI systems like DENDRAL and MYCIN ^{19,22} ; Bayesian networks by Judea Pearl ²³ ; principal component analysis advances by Pearson ²⁴ and Hotelling ²⁵ ; support vector machines by Vapnik and Chervonenkis. ²⁶
1970s	Development of genetic algorithms by Holland ²⁷ ; popularization of clustering techniques by MacQueen ²⁸ ; further development of logic programming and constraint satisfaction problems.
1980s	Ensemble learning methods like bagging and boosting; backpropagation introduced by Rumelhart, Hinton, and Williams ²⁹ ; structural causal models by Pearl. ³⁰
1990s	Development of reinforcement learning frameworks like Q-learning and policy gradient methods ³¹ ; prominence of Hidden Markov models by Rabiner. ³²
2000s	Introduction of generative adversarial networks by Goodfellow ³³ ; emergence of diffusion models ³⁴ ; popularization of deep learning by LeCun, Bengio, and Hinton ³⁵ ; advances in differential privacy by Dwork. ³⁶
2010s	Development of variational autoencoders by Kingma and Welling ³⁷ ; revolution in natural language processing by attention mechanisms and transformers ^{38,39} ; introduction of frameworks like Google’s AutoML ⁴⁰ ; advances in Explainable AI driven by DARPA ⁴¹ ; breakthroughs with Google AlphaGo ⁴² and AlphaFold. ⁴³
2020s	Popularization of the term “stochastic parrots” by Bender et al ⁴⁴ highlighting limitations and ethical considerations of large language models; rise of AI-powered conversational agents like ChatGPT and Claude.

History of innovation cascades leading to AI applications, originating from deeper understandings of logic and causal reasoning, mathematics, statistics, hypothesis testing, and various ML “tribes” and other tools under the umbrella term of AI.
Abbreviations: ANOVA = analysis of variance; AI = artificial intelligence; ML = machine learning.

sequentially. Parallel processing capability has rapidly advanced the field of NLP and underpins large language models (LLMs) like ChatGPT, used in many applications, including neurology practice, research, and education. The “*Stochastic Parrots*” paper raised concerns about this evolution, emphasizing the ethical implications and limitations of LLMs, urging caution (see part 2).⁴⁴

Spectacular AI innovations continue to spring from human imagination, reasoned exploration of hypothetical and counterfactual “what if” scenarios (see “AI and Causation” section), open-ended discussion, and determined

experimentation. These advances are revolutionizing the neurological sciences and unlocking new insights into the complex workings of the brain and healthcare systems.

AI Varieties

AI varieties include ML and older established approaches rooted in traditional computer programming and computer science (Fig S1). ML is a prominent subset of modern AI. In “The Master Algorithm,” Domingos⁵³ classifies ML into 5 “tribes”, symbolists, connectionists, evolutionaries,

Bayesians, and analogizers, each offering unique methodologies with significant implications for neurological care, research, and education (Table 2A). Symbolists use logic and symbols to represent knowledge and make inferences, relying on inductive logic programming and other methods.^{65,66} In neurology, symbolists develop diagnostic decision support systems that identify conditions based on patient symptoms and medical history (e.g., diagnosing multiple sclerosis or epilepsy).⁵⁵ Connectionists, inspired by the brain's neural networks, adjust weights in neural network connections based on input–output pairs.^{17,60} This approach, including deep learning, effectively processes medical images, like MRI and CT scans, detecting anomalies and diagnosing tumors or strokes.

Evolutionaries use algorithms inspired by natural selection, such as genetic algorithms, to optimize solutions. In neurology, these methods customize treatment plans and personalize therapy based on genetic and clinical data^{27,67} (e.g., optimizing treatment for chronic pain).⁵⁷ Bayesians apply Bayes' theorem to update the probability of hypotheses and model parameter estimates as more evidence becomes available. Bayesian methods are useful in neurology for probabilistic reasoning in diagnosis and treatment, incorporating prior knowledge and new evidence to predict disease progression and treatment efficacy.^{30,68} Analogizers learn by drawing analogies between similar instances, using techniques like support vector machines and nearest neighbor algorithms.^{26,108} Analogizers classify neurological conditions based on similarities with previously diagnosed cases, aiding in the early detection of neurological diseases.

Although Domingos classifies ML varieties, LeCun et al focus on how ML algorithms learn from data or interactions,³⁵ categorized into supervised, unsupervised, and reinforcement learning, particularly suited to DNNs with multiple layers that model complex patterns and representations in data (see “Artificial Neural Network Anatomy and Applications” section). Russell and Norvig⁶⁰ and Poole and Mackworth⁶⁷ provide broader taxonomies and additional foundational perspectives on ML/AI (Table S1).

Several key AI approaches predate ML, including expert systems, search algorithms, logic programming, optimization algorithms, symbolic AI, planning, rule-based systems, and constraint satisfaction problems (Table 2B). Classical approaches often complement newer AI paradigms, like ML and deep learning, enhancing robustness, interpretability, and effectiveness in solving contemporary problems in neurology and other fields.^{60,61,69} Researchers combine approaches to create hybrid or ensemble models, improving their ability to diagnose, treat, and manage neurological conditions. Applications span NLP, planning and scheduling, predictive analytics, computer vision, robotics, speech processing, and more.

Although these applications demonstrate AI's current capabilities, its foundations in computer science and mathematics are equally important for understanding its limitations and potential in neurology. For instance, the “polynomial time (P) vs nondeterministic polynomial time (NP)” problem,⁷⁰ is a fundamental challenge in AI and computer science, addressing how efficiently problems can be verified and solved. The relevance of this problem becomes evident when tackling the computational challenges posed by large and complex datasets in neurology. These datasets or “data lakes” (discussed in part 3) are being aggregated by nationwide consortia focused on intensively studied neurologic conditions like stroke, Parkinson's disease, Alzheimer's disease, and related disorders. Currently, AI addresses such complex problems through approximations and heuristics, which are effective but suboptimal. Advances like quantum computing may one day provide the breakthroughs needed to tackle the “P vs NP” problem directly, unlocking new possibilities for neurology, such as personalized medicine and complex disease modeling.

Many of the scientific underpinnings of AI—such as linear algebra, calculus, probability, and statistics—likely align with neurologists' academic backgrounds. Ananthaswamy's “*Why Machines Learn*”⁷¹ offers accessible explanations of how these principles underpin ML and contrast its data-driven learning approach with traditional rules-based computer programming.⁶⁰

AI and Laws of Thought

AI, like neurology and neuroscience, is deeply rooted in philosophy, psychology, and logic, leveraging deductive, inductive, and abductive reasoning. These forms of reasoning, integral to human practitioners and AI systems dedicated to advancing neurological care, education, and research, deserve greater understanding and critical review to maximize their potential.

Deductive reasoning draws certain conclusions if the premises are correct. Socrates deduced, “All men are mortal. Socrates is a man. Therefore, Socrates is mortal.” Descartes famously stated, “*Cogito ergo sum*” (I think, therefore I am). Although central to mathematical proofs, deduction is not the primary mode for subtle diagnostics, which often require a blend of reasoning methods.

Induction generalizes from specific observations to generate probabilistic conclusions. David Hume argued that inductive reasoning arises from custom and habit, but that we can never truly know if one event causes another.⁷² Karl Popper asserted that induction has no place in the logic of science.⁷³ Nevertheless,

TABLE 2. AI Varieties

(A) Five tribes of AI

Tribe	Key algorithmic methods	Neurology applications
Symbolic	Decision trees, rule-based systems, knowledge graphs, inverse deduction, random forest	Diagnostic decision support systems for diagnosing diseases like multiple sclerosis or epilepsy ⁵⁵
Connectionist	Artificial neural networks, deep learning, convolutional neural networks, backpropagation	Processing medical images (MRI, CT scans), detecting anomalies, diagnosing tumors or strokes ⁵⁶
Evolutionary	Genetic algorithms, evolutionary strategies, genetic programming	Customizing treatment plans, for example, optimizing spinal cord stimulation for treating chronic pain ⁵⁷
Bayesian	Bayesian networks, Bayesian optimization, Gaussian processes, Bayesian Inference	Probabilistic reasoning for patient diagnosis and treatment, predicting disease progression ⁵⁸
Analogizers	Case-based reasoning, analogical reasoning, similarity-based learning, support vector machines	Classifying neurological conditions, early detection of rare diseases, Alzheimer's disease, seizure classification in epilepsy ⁵⁹

(B) Classical AI tools

Technique	Algorithms	Description and/or neurology applications
Expert systems (1960s)	Rule-based algorithms, inference engines	Uses rules and logic to mimic human decision-making, ²² aid in diagnosing diseases, like multiple sclerosis or epilepsy
Search algorithms (1950s)	Breadth-first search, depth-first search, A* algorithm, Dijkstra's algorithm	Navigate problem spaces to find optimal solutions, ⁶⁰ such as surgical paths or neuroimaging data analysis
Logic programming (1970s)	Resolution, unification, backtracking	Infers conclusions from rules and facts, ⁵⁴ modeling neurological knowledge for diagnosis based on symptoms and medical history
Optimization algorithms (1950s)	Genetic algorithms, simulated annealing, particle swarm optimization, gradient descent	Identify the best solutions among many possibilities, ²⁷ like optimizing treatment plans for neurological disorders
Symbolic AI (1950s)	Semantic networks, knowledge representation frameworks, ontology-based algorithms	Manipulates symbols for tasks, such as natural language processing of neurological research literature, ⁶¹ including semantic networks and knowledge graphs
Planning (1960s)	STRIPS partial-order planning, hierarchical task network planning	Creating action sequences to achieve goals, ⁶² such as automated systems planning patient care pathways or rehabilitation protocols
Rule-based systems (1970s)	Forward chaining, backward chaining	Derive conclusions or perform actions using “if-then” rules, ⁶³ as seen in clinical decision support systems guiding diagnoses and treatments
Constraint satisfaction problems (1970s)	Backtracking, constraint propagation, local search algorithms, arc consistency algorithms	Solve issues defined by constraints, ⁶⁴ such as scheduling patient appointments or resource allocation in neurology departments

This table highlights foundational AI methods and their applications in neurology. (A) Five tribes of machine learning with key algorithmic methods and neurology applications.^{53,54} (B) Classical AI tools from traditional computer science, detailing their introduction dates, algorithms, descriptions, and neurology applications

Abbreviations: AI = artificial intelligence; CT = computed tomography; MRI = magnetic resonance imaging; STRIPS = Stanford Research Institute Problem Solver.

neuroscientists apply induction to generate hypotheses they test by experimentation, which can be rejected but never fully confirmed. Induction's limitation, the empirical constraint, can lead to flawed conclusions from novel encounters. For example, a neurologist might misdiagnose rare disorders as common conditions based on past experiences—a “black swan” scenario.⁷⁴ Similarly, an AI algorithm relying on typical cases might miss atypical situations, akin to Russell's inductivist turkey, which, being fed every day, failed to anticipate its eventual slaughter. Dealing with ambiguous or unusual neurological presentations benefits from an open mindset, intellectual integrity, avoiding inductive biases, and exploring alternative hypotheses through abductive reasoning.^{75,76}

Abduction, coined by Charles Sanders Peirce, infers preconditions from consequences and making educated guesses about causes.⁷⁷ Abduction is crucial for diagnosing complex neurological disorders by forming hypotheses to explain atypical symptoms that do not fit known patterns. This requires synthesizing information, considering multiple explanations, and using deep neurological knowledge. Abduction helps identify faults or factors that likely cause problems, refined through successive observations, following the principles of probabilistic inference of Reverend Thomas Bayes (*b*, 1701, $P = 0.75$, as the data show).⁷⁸ Human experts' abductive reasoning currently surpasses AI, which excels at pattern recognition but struggles with nuanced reasoning and creative problem-solving in complex cases.

AI's logical reasoning capacities are advancing through ML research and deeper explorations of causal inference (see “AI and Causation” section). For example, case-based reasoning systems may potentially improve AI's abductive capabilities by storing libraries of past cases and using similarity metrics to retrieve the most relevant examples for new problems.^{79,80} Combining neural networks with symbolic logic are being investigated to integrate pattern recognition with explicit reasoning.⁸¹ AI tools assist neurological diagnosis, such as analyzing brain scans for abnormalities and enhancing diagnostic reasoning through the integration of ML and symbolic approaches.^{81,82} However, these tend to focus on specific narrow tasks rather than holistic clinical reasoning.

AI is increasingly valuable for augmenting neurologists' reasoning, especially in complex cases requiring extensive information synthesis. Human expertise is crucial for supervising AI and contextualizing insights, enhancing diagnosis, and patient care. Key challenges include handling heterogeneous clinical data, modeling uncertainty, promoting generalizability, avoiding overfitting, incorporating background knowledge, improving efficiency, and ensuring transparency and explainability to foster clinician trust. Understanding

and mitigating AI biases in reasoning are fundamental to all applications.⁸³

AI and Bias in Logical Reasoning

Bias in logical reasoning challenges humans and AI. Logic helps human brains and AI explain complex, ambiguous data and situations. Explanatory models start from hunches and rely on assumptions that may never be proven.⁸⁴

Beliefs affect human interpretations and conclusions based on facts and evidence. Confirmation bias (Fig S2) is the tendency to seek and prefer information that supports our beliefs while ignoring contradictory data.⁷⁶ Understanding how emotions bias us is crucial for logical decision-making and civil argumentation.⁸⁵ Recognizing our belief systems and mitigating biases, such as the notion that AI is dangerous, is essential.^{86,87}

AI can develop biases (Table S2), even without human emotion or investment in beliefs, based on poor training or unsound assumptions. Obermeyer et al⁸⁸ highlighted significant racial bias in a widely used healthcare algorithm, relevant to neurology, underscoring this issue. Understanding and addressing these biases is crucial for developing fair and equitable AI systems.

AI and Causation

Understanding principles of causal inference is central to neurology and AI, enabling researchers and clinicians to identify true cause-and-effect relationships in complex neurological systems, model brain function more accurately, deepen understanding of disease mechanisms, enhance diagnostic tools, and develop effective personalized treatments and public health strategies.

Pearl and Mackenzie⁸⁹ envisioned a 3-rung ladder of causation, essentially “seeing, doing, imagining,” which frames our understanding of AI capabilities and neurological applications (Fig S3). The first rung involves learning by association, a capability of current AI and most animals. The second rung pertains to learning the effects of specific actions, like how babies acquire causal knowledge. The top rung, counterfactual learners, can imagine worlds that do not exist and infer reasons for observed phenomena, pondering “What if?” and “If only?” Capable AI should reason at all levels.

AI-emulated deduction, induction, and abduction reasoning (see “AI and Laws of Thought” section) map onto Pearl's ladder (Table S3). Deduction derives causal relationships from assumptions or causal models,⁹⁰ fitting at lower rungs. Induction falls in the middle, generating causal models to learn from data and make predictions. Abduction occupies the top rung, developing and refining

causal models, including counterfactual propositions and hypotheses.

Classical statistics, which predate and contribute to AI (“AI and Synergies with Biostatistics” section), can also be contextualized within Pearl’s ladder of causation. At the bottom rung, classical statistical analyses assess parameters of a distribution from samples to infer associations among variables⁹¹ (e.g., correlation, linear regression, and risk ratios), which generally do not address causal concepts except for situations like randomized clinical trials. Methods like instrumental variables, propensity score matching, and structure equation models^{92–95} advance the framework to the middle rung. The counterfactual top rung tackles complex causal questions, such as, “Does traumatic brain injury cause Alzheimer’s disease?” (see example below), which requires sophisticated tools and methodologies that extend beyond simple associations. Causal analyses infer probabilities under changing conditions, beyond methods that rely solely on the joint or distributional distribution of observed variables, such as correlation or regression. Causal concepts—at the upper rungs of Pearl’s ladder—require an understanding of interventions and dynamic changes that basic statistical methods at the lowest rung do not capture (Data S1).⁹¹

Although Pearl’s framework helps explain AI capabilities, emerging AI tools are bridging gaps across Pearl’s ladder, creating a cycle of progress. AI-driven causal algorithms are transforming neurological diagnosis, care, and treatment by clarifying causal relationships among key factors, such as genetics, environment, and lifestyle across a patient’s lifespan. These tools are unravelling the complexities of Alzheimer’s⁹⁶ and Parkinson’s⁹⁷ diseases. Bayesian causal models⁹⁸ and probabilistic causal reasoning improve inferences despite measurement errors or incomplete patient histories,⁹⁹ enhancing diagnostic accuracy. Causal transfer and generalization methods enhance model adaptability across diverse patients and populations. Causal models support better decision-making in treatment options and lifestyle interventions—such as critical care strategies^{83,100}—and informing public health policies to preserve cognitive function.

Modern neuroepidemiology often combines emerging AI tools and advanced causal reasoning, such as Pearl’s approach, with traditional heuristics, like Hill’s criteria, to rigorously assess potential causal relationships. Neurologists may recall Sir Austin Bradford Hill’s principles of causality, which include strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experimental evidence, and analogy.¹⁰¹ These principles assess causality without formal modeling, as exemplified by studies linking tobacco to cancer.¹⁰² However, their flexibility can lead to subjective interpretations,

particularly regarding specificity. Single causes can exert multiple effects, and single effects may arise from multiple causes, complicating the isolation of clear causal pathways. In neurology, for example, Hill’s criteria can explore associations between traumatic brain injury and Alzheimer’s disease. Although strength, consistency, temporality, and experimental evidence are relevant, specificity is less critical because of traumatic brain injury’s multiple potential outcomes and complex causal pathways. In contrast, Pearl’s approach offers deeper insights by modeling interventions and exploring hypothetical outcomes through mathematical and graphical tools, like Bayesian networks and do-calculus. This allows a more rigorous analysis of causality, surpassing the observational focus of Hill’s criteria.

AI techniques enhance both Pearl’s and Hill’s frameworks. For Hill’s criteria, methods like supervised learning, regression, meta-analysis algorithms, clustering, temporal models, graphical models, simulation models, and knowledge graphs contribute to various aspects of causal assessment. Pearl’s approach benefits from AI-driven pattern identification, reinforcement learning, and causal inference algorithms for interventions and applies counterfactual models for scenario simulation. Together these AI integrations make causal analysis more precise and comprehensive, for clearer understanding of complex neurological relationships. Causal inferences on the effects of interventions from observational studies are a critical topic in healthcare.¹⁰³ Bareinboim et al¹⁰⁴ discuss how integrating causal reasoning into AI systems can enhance fairness and transparency.

AI and Synergies with Biostatistics

AI tools and classical statistics are increasingly intertwined, complementing each other to greatly benefit the neurological sciences (Table S4). Neurologists and neuroscientists have traditionally collaborated with biostatisticians to design studies and analyze data, including prespecified statistical plans, hypotheses, outcome and control variables, methods, and data presentation to avoid “fishing” and to mitigate false-positive findings.¹⁰⁵

Classical statistical methods assume a probabilistic data model to relate predictors to outcomes, known as the “Data Modeling Culture.”¹⁰⁶ Model validation is typically performed by goodness-of-fit tests, examining residuals, and hypothesis testing. These methods rely on George Box’s adage, “All models are wrong; some are useful,” which also applies to AI. For example, in a study on how age predicts cognitive levels in elderly individuals, a simple linear regression model might capture the essence of the data over certain age ranges (Pearl level 1). Interpreting results can be straightforward, such as the average change in cognition per year of age. However, the linear

relationship might be too simple to accurately predict or extrapolate. Additionally, the results assume normality of the residuals, which technically is not possible unless the cognitive metric is unbounded.

High-dimensional data, common in neuroscience, often overwhelm conventional statistical methods.¹⁰⁷ Classical methods like regression analysis and survival analysis can struggle to handle the complexity and volume of modern neurological data sets. The K-nearest neighbors (KNN) algorithm,¹⁰⁸ a simple yet powerful non-parametric method, bridges the domains of statistics, geometry, and ML. However, KNN faces challenges in high-dimensional spaces, where distance metrics like Euclidean or Manhattan distance (between neighboring points in a grid-like Manhattan's) lose their discriminative power because of the aforementioned “curse of dimensionality.” In these spaces, data points tend to become equidistant, making it difficult for KNN to distinguish between neighbors. This issue arises in brain imaging applications, such as functional MRI or diffusion tensor imaging analysis of Alzheimer's disease, where the complexity of the data requires advanced AI techniques to extract meaningful patterns and predict disease progression.

Statistical approaches are evolving alongside AI to tackle the “curse of dimensionality.” Techniques like least absolute shrinkage and selection operator, or LASSO, have become routine for analyzing high-dimensional data without preliminary dimension reduction.¹⁰⁹ Adaptive modeling and data assimilation techniques can enhance model accuracy in complex systems.¹¹⁰ Smoothed online learning tools¹¹¹ can manage high-dimensional data in real-time, augmenting traditional statistical methods.

The “Algorithmic Modeling Culture” uses AI tools that permit the relationship between predictors and outcomes to be complex and unknown.¹¹² Whereas classical statistical tools generally handle more static datasets, AI handles high-dimensional, dynamic, time-sensitive datasets that continuously evolve, discovering patterns that conventional methods might miss. Nevertheless, core AI methods, such as model training, testing, and validation, depend on classical statistics. In turn, AI tools enhance the entire data workflow (Fig 2), serving as inputs for these statistical methods (Fig S4). Models are validated by their predictive accuracy, preferably using test datasets not used to build and train the model. However, overfitting remains a key challenge in neuroscience AI applications.

Overfitting occurs when a model performs well on training data, but poorly on new, unseen data because it has fit the noise and random fluctuations in the training set in addition to the genuine underlying patterns (Fig S5). This often occurs from overparameterization (i.e., model has more parameters than necessary to fit the

data) leading to excessive flexibility in capturing specific anomalies rather than general patterns (see “Artificial Neural Network Anatomy and Applications” section). Interestingly, the human brain learns efficiently from limited examples, suggesting it possesses inductive biases—built-in tendencies to favor certain solutions—that help avoid the pitfalls of overparameterization often seen in AI models.¹¹³ By studying these inductive biases, researchers may develop AI models that generalize better from small datasets, improving performance and robustness.

Useful models must generalize well to new data, across different patients or brain scans. Techniques like cross-validation (e.g., k-fold or leave-one-out) robustly assess model performance and mitigate overfitting risks. Additional methods, such as early stopping, data augmentation, ensemble methods, dropout, and regularization, enhance model robustness and generalization.¹¹⁴ Transfer learning allows models to leverage knowledge from other tasks, using pre-trained networks fine-tuned for specific applications, reducing the risk of overfitting and improving generalization.¹¹³

Underfitting occurs when the model is too simple to learn patterns in the data, resulting in poor performance on both training and new data. This can be mitigated by increasing model parameters and extending training.¹¹⁵

Overall, the neurological sciences and other fields benefit from integrating biostatistical techniques with AI-driven designs and mathematical approaches.¹¹⁶ As both fields continue to evolve,¹¹⁷ more statisticians are training in AI tools, fostering collaborations that facilitate robust analyses and enhance the understanding and care of neurological conditions.

Neural Networks: History and Underpinnings

AI draws heavily on analogies to the nervous system and key neurological concepts, making it a special focus and pride of the neurological sciences. Neural networks (Fig S6) underpin many modern AI algorithms, tracing their origins to McCulloch and Pitts' 1943 paper, “A Logical Calculus of the Ideas Immanent in Nervous Activity.”¹⁷ They modeled neurons as binary devices that do or do not fire based on their inputs, creating a neural activity model using logic gates, which laid the theoretical foundation for artificial neural networks. Subsequently, Donald Hebb, often regarded as a “father of neuropsychology,” proposed his influential theory in 1949 that neural connections strengthen when neurons fire together, underpinning neural plasticity and brain learning.¹⁸

Next, Frank Rosenblatt²¹ designed the perceptron, which had a single layer (i.e., an input layer, not counted in the original perceptron model, with a single output layer and no hidden layers) and introduced adjustable

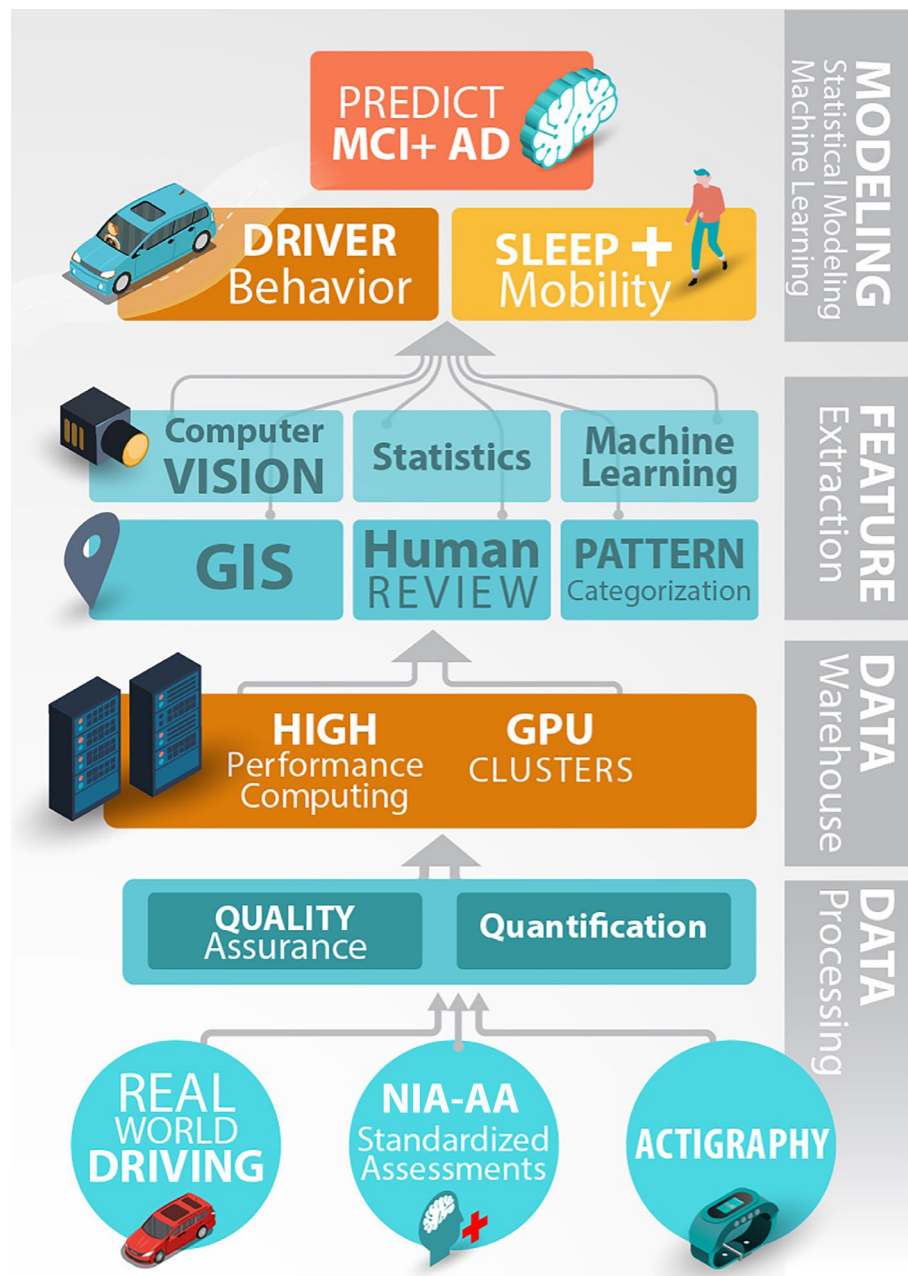


FIGURE 2: Workflow diagram combining classical biostatistical techniques with artificial intelligence (AI)/machine learning (ML) in neurology. Modern workflow that combines biostatistical methods with AI and ML to analyze real-world data. This approach examines the impact of neurological conditions on real-world functioning, capturing the “brain in the wild,” and predicting diseases using novel phenotypes from digital biomarkers. The process starts with collecting data from sources like patient demographics, medical assessments, functional abilities, and real-world behavioral and physiological data, which is then organized, cleaned, and synchronized for analysis. Multivariate and ML techniques are used, incorporating computer vision, statistical analysis, geographic information systems (GIS), human review, and pattern categorization. Large datasets are processed efficiently using high-performance computing and graphics processing unit (GPU) clusters, with quality assurance to ensure accuracy and reliability. Applications include medical diagnostics, disease progression prediction, treatment efficacy assessment, safety evaluations, social interaction analysis, lifespace assessments, and quality-of-life measurements. By integrating statistical analysis, design methodologies, and AI/ML, this approach enhances the understanding of neurological disorders and improves patient outcomes. MCI, mild cognitive impairment; AD, Alzheimer’s disease; NIA-AA, National Institute on Aging and Alzheimer’s Association. [Color figure can be viewed at www.annalsofneurology.org]

weights. Although the perceptron also operated with binary inputs and outputs, its learning rule for adjusting weights was flexible compared to the McCulloch-Pitts model, which did not include learning or weight adjustment. In

1969, Minsky and Papert¹¹⁸ published “*Perceptrons: An Introduction to Computational Geometry*,” a critical analysis of single-layer perceptrons. These networks could not solve some problems, like the exclusive OR (XOR) function,

which outputs “true” only when 2 inputs differ, a limitation stemming from their reliance on linear separation, making them incapable of recognizing non-linear patterns. The analysis underscored the need for more advanced architectures, such as multi-layer perceptrons, which incorporate hidden layers and activation functions to process non-linear patterns and solve complex real-world problems.

Although Rosenblatt had already begun exploring multi-layer perceptrons, effective training methods were not yet available, reinforcing Minsky and Papert’s skepticism and lowering interest in and funding for neural network research. Rosenblatt’s pioneering work ultimately laid the foundation for modern deep learning, but his tragic death in a boating accident in 1971 left many of his ideas unrealized. This period of doubt contributed to the “AI winter” of the late 1970s and early 1980s, with stalled progress in neural networks until more advanced methods and computational power reignited interest.

AI rebounded powerfully in the 1980s when advances such as backpropagation and increased computational power enabled more effective training of complex neural networks. Interest surged with new architectures, like Hopfield networks (Data S1),¹¹⁹ using binary units inspired by McCulloch-Pitts’ neurons, and Hebbian learning to facilitate pattern storage and recognition.

The remarkable scientific journey from McCulloch and Pitts, through Hebb, Rosenblatt, and early perceptrons to modern deep learning showcases the vibrancy and evolution of AI. Today, neural networks drive breakthroughs in computer vision, NLP, and reinforcement learning, although also advancing numerous impactful neurological applications (reviewed in parts 2 and 3). To crown these brilliant scientific achievements, John Hopfield and Geoffrey Hinton were awarded the 2024 Nobel Prize in Physics “for foundational discoveries and inventions enabling machine learning with artificial neural networks.”¹²⁰

Artificial Neural Network Anatomy and Applications

A neural network consists of interconnected nodes, analogous to neurons, organized into layers: an input layer receives data, hidden layers perform computations, and an output layer produces results (Fig S6, Table S1). Simple neural networks have 1 or 2 hidden layers, whereas deep learning systems have multiple hidden layers, increasing complexity and power, but diminishing explainability of its operations.³⁵ Neural networks learn through “back-propagation”²⁹ of errors between predicted and actual outcomes, which feedback to adjust synaptic weights to improve performance. An activation function, applied to each neuron’s output, introduces non-linearity, allowing

the network to learn complex patterns in the data. Early neural networks used the sigmoid function, which could cause the gradient vanishing problem during back-propagation, making it difficult for the network to update weights effectively, especially in deep networks. Modern systems use the rectified linear unit function to mitigate this issue, more effectively training deep networks.

Different network structures enhance capabilities for various tasks. Deep learning models depend on DNNs, includes CNNs, RNNs, and generative AI like GANs and LLMs, with distinct structures and uses (Table 3). CNNs, designed for grid-like data, excel in image tasks. RNNs handle sequential data, making them ideal for language modeling and time series. GANs generate realistic data, often used in image synthesis. LLMs, based on transformers, excel in NLP, like translation and summarization. Complex deep learning models, such as DNNs, CNNs, GANs, and LLMs, are at risk of overparameterization, typically because they have a large number of weights and biases. This can lead to overfitting, which can be mitigated through approaches such as transfer learning mentioned (see “AI and Synergies with Biostatistics” section).

Deep learning models have many applications in neurology, neurological science, and healthcare systems (Table 3). For instance, NLP analyzes clinical notes and patient records, predictive analytics forecast disease progression and treatment outcomes, and speech recognition aids patients with communication disorders. These diverse applications underscore the broad potential of neural networks to enhance various aspects of neurological care and research.

Computer vision is a pivotal application that leverages complex neural networks to interpret and make decisions based on visual data (Table 4). The process typically involves image acquisition, preprocessing to enhance quality and remove noise, feature extraction, object detection and recognition, and interpretation based on spatial relationships. CNNs are central to this method, processing images through multiple layers that extract increasingly complex features. CNNs and DNNs trained on labeled visual data identify patterns, edges, shapes, and features, refining their parameters through backpropagation to enhance performance.¹³⁰

CNNs process input data through local receptive fields and apply filters at different resolutions, creating a feature map for efficient analysis. This architecture mimics the hierarchical structure of the human visual cortex, inspired by how neurons respond to visual stimuli.^{35,145} CNNs can have hundreds of layers, each learning to detect increasingly complex image features,⁴⁶ essential for recognizing faces, gaits, or medical images like gliomas, melanomas, or edematous retinas.

AI models such as you only look once, region-based convolutional neural network, and single shot multiBox

TABLE 3. Deep Learning Models in Healthcare

Model type (yr)	Structure	Algorithms used	Use cases	Key characteristics	Examples in neurology and neurosurgery
Feedforward neural networks (1940s–1970s)	Input layer, 1 or more hidden layers, output layer. Fully connected neurons	Backpropagation, gradient descent	General-purpose tasks, regression, classification	Started shallow; no cycles or loops; information flows forward ¹²¹	Predicting patient outcomes based on clinical data
Convolutional neural networks (1980s)	Convolutional layers, pooling layers, fully connected layers	Convolutional algorithms, pooling algorithms, backpropagation	Image and video recognition, object detection, segmentation	Captures spatial hierarchies and local patterns in data ³⁵	MRI and CT scan analysis for tumor detection
RNNs (1980s)	Cyclic connections with hidden state	BPTT, truncated BPTT	Sequential data, time series forecasting, language modeling, speech recognition	Processes variable-length sequences, suffers from vanishing/exploding gradients ¹²²	Analyzing sequential brainwave data for seizure prediction
Autoencoders (1980s)	Encoder compresses input, decoder reconstructs input	Backpropagation, gradient descent	Dimensionality reduction, denoising, anomaly detection	Learns compact data representation, captures essential features ¹²³	Identifying abnormalities in neuroimaging data
RBM (1986)	Two-layer neural network, consisting of a visible layer and a hidden layer	Contrastive divergence, Gibbs sampling	Feature learning, dimensionality reduction	Learns a probability distribution over its set of inputs ^{121,123}	Learning features from neuroimaging data
LSTMs (1997)	Special RNN with input, forget, and output gates	LSTM cell algorithms, BPTT	Sequential data with long-term dependencies, text, time series	Handles long-term dependencies, mitigates vanishing gradient problem ¹²⁴	Predicting disease progression from longitudinal patient data
Graph neural networks (2005)	Operates on graph-structured data	Graph convolutional algorithms, message passing algorithms	Social network analysis, molecular structure prediction, recommendation systems	Captures dependencies and patterns in graph data ¹²⁵	Modeling brain connectivity networks and their abnormalities
Deep belief networks (2006)	Stacked RBMs, where each layer's hidden units are treated as visible units for the next	Contrastive divergence, Gibbs sampling	Feature learning, generative modeling	Combines multiple RBMs, capable of learning hierarchical representations ⁴⁵	Analyzing neuroimaging data for brain disorders
VAEs ^a (2013)	Autoencoder with probabilistic latent variable models	Stochastic gradient descent, variational inference	Generative tasks, data sample generation	Combines autoencoders with probabilistic modeling ⁵²	Generating synthetic brain images for data augmentation
Deep reinforcement learning (2013)	Neural networks combined with reinforcement learning	Q-learning, policy gradients, deep Q-networks	Game playing, robotic control, autonomous vehicles	Learns optimal actions through trial and error	Optimizing surgical robot control in neurosurgery ¹²⁶
GANs ^a (2014)	Generator and discriminator in competition	Adversarial training, backpropagation, gradient descent	Generating realistic data samples (images, videos, audio)	Capable of producing high-quality synthetic data, challenging to train ⁵¹	Creating realistic synthetic neuroimaging data for training models
GRUs (2014)	Simplified LSTM with fewer gates	GRU cell algorithms, BPTT	Sequential data tasks like LSTMs	Computationally more efficient than LSTMs with similar performance ¹²⁷	Modeling patient recovery trajectories after neurosurgery
Transformer networks ^a (2017)	Self-attention mechanisms, processes data in parallel	Self-attention mechanisms, multi-head attention, position-wise feed-forward networks	Natural language processing, machine translation, text generation, sentiment analysis	Efficient at handling long-range dependencies, scalable to large models ³⁸	Interpreting clinical notes and patient records for diagnosis support
Capsule networks (2017)	Layers of capsules that output vectors (instantiation parameters) rather than scalars	Dynamic routing algorithms	Image recognition, object detection	Encodes spatial hierarchies in data, robust to affine transformations ¹²⁸	Brain tumor classification from MRI scans
Diffusion models ^a (2020)	Iteratively refine random noise to generate data by reversing a diffusion process	Denoising diffusion probabilistic models	Generative tasks, high-quality image synthesis, data augmentation	Capable of generating high-quality images, different approach to generation compared to GANs and VAEs ¹²⁹	Generating realistic neuroimaging data for enhancing training datasets

Summary of deep learning models, including year introduced, structural components, commonly used algorithms, use cases, key characteristics, examples in neurology/neurosurgery, and references. The overview addresses each model type's function and relevance in medical applications.

^aGenerative models include transformers, autoencoders, GANs, VAE, and diffusion models, which have seen marked development or popularization in recent years, having conceptual origins or predecessors from earlier periods.

Abbreviations: BPTT = backpropagation through time; CT = computed tomography; GAN = generative adversarial networks; GRU = gated recurrent units; LSTMN = long short-term memory networks; MRI = magnetic resonance imaging; RBM = restricted Boltzmann machines; RNN = recurrent neural networks; VAE = variational autoencoders.

TABLE 4. Applications of AI Computer Vision in Neurology

Application	Description
Automated diagnosis of neurological disorders	Using brain MRI or CT scans to diagnose Alzheimer's disease, Parkinson's disease, and multiple sclerosis ^{130–132}
Quantitative analysis of brain lesions and atrophy	Analyzing brain lesions and atrophy in neurological conditions ^{133,134}
Segmentation and volume estimation of brain structures	Segmenting and estimating the volume of brain structures, such as the hippocampus and ventricles ¹³⁵
Detection and monitoring of cerebral microbleeds and microvascular disease	Predict evolution of white matter intensities in brain MRI ¹³⁴
Analysis of retinal images	Early detection of neurological disorders using retinal images ^{136,137}
Intraoperative guidance during neurosurgery	Using computer vision techniques for guidance during neurosurgery and follow up brain imaging ^{138,139}
Tracking eye movements and gaze patterns	Diagnosing and monitoring neurological conditions by tracking eye movements and gaze patterns ¹⁴⁰
Automated analysis of neuronal morphology and connectivity	Analyzing neuronal morphology and connectivity in microscopy images ^{156,157,179}
Quantification of gait and movement disorders	Using video analysis to quantify gait and movement disorders ^{141,142}
Facial expression recognition	Assessing neurological conditions affecting facial muscles through facial expression recognition ^{143,144}

Computer vision uses AI algorithms to automatically process and extract insights from images and videos, with powerful applications in neurology. For instance, AI has significantly advanced MRI technology by enabling image reconstruction from under sampled data, thereby reducing scan times. It also enhances image quality by minimizing noise and artifacts, supports automated lesion detection for identifying tumors, ischemia, and multiple sclerosis plaques, and optimizes sequence protocols for patient-specific clinical applications

Abbreviations: AI = artificial intelligence; CT = computed tomography; MRI = magnetic resonance imaging.

detector detect and localize objects in images or videos, providing categories and positions via bounding boxes. Semantic segmentation assigns class labels to image pixels using fully convolutional networks and encoder-decoder architectures.¹²⁷ U-Net is widely used in medical imaging for its ability to handle small datasets and capture fine structures.¹⁴⁷

Versatile neural network applications extend to various domains, including autonomous vehicles, surveillance systems, and robotics. Neurologists and other healthcare professionals must select the appropriate tools for their specific tasks to maximize the benefits of these advanced AI technologies.

AI Model Selection and Process Flow in Neurology

Selecting AI models in neurology (Fig S4, Table S5) depends on data characteristics, such as structure, size, noise, missing values, and distribution.¹⁴⁸ Models serve various purposes: regression for continuous variables, classification for categorical outcomes, clustering for patterns, dimensionality reduction for feature selection, time series for temporal data, deep

learning for complex patterns, and NLP for text analysis.¹⁴⁹

AI can also aid in defining the research question, for instance through NLP, which can help review literature to identify gaps and trends, making research data-driven. AI can also gather diverse neurological data, such as MRI/CT scans, electroencephalography (EEG)/magnetoencephalography (MEG) signals, genetic information, and clinical records.

Researchers, with the help of AI, preprocess data for quality control.¹³¹ MRI/CT scans are normalized and the skull is stripped, artifacts are removed and features extracted from EEG/MEG signals,¹⁵⁰ and features are selected from genetic data.¹⁴⁶ Statistical methods and AI algorithms handle missing data and noise. Deep learning automates imaging processes and AI-driven feature extraction identifies biomarkers.¹⁴⁶ Clinical data integration provides a comprehensive patient view.

For model building, data are split into training, validation, and test sets (e.g., 60–80% for training, 10–20% for validation, and 10–20% for testing). Supervised learning predicts outcomes for labeled data, ideal for classifying disorders¹³³ and prognosis prediction.¹³⁴ Unsupervised learning

identifies patterns in unlabeled data, which is useful for brain network clusters^{157,158} and neuroimaging data reduction. Reinforcement learning trains models through reward-based decision-making,^{161,163} which is useful in robotics and adaptive treatments. Masked autoencoders use self-supervised learning to improve efficiency and accuracy, particularly in image and NLP tasks.¹⁵¹ Hybrid models adapt to various use cases.

Models are refined through hyperparameter tuning,¹⁵² feature selection,¹³⁶ cross-validation, and algorithm selection.^{115,152,153} These hyperparameters influence how the model learns patterns from data and impact its overall performance. Examples of hyperparameters in DNNs include the learning rate, batch size, number of epochs (times the DNN processes the entire dataset), number of layers, number of

neurons per layer, dropout rate, activation function, and optimizer, all of which are set to control the learning process.

The generalizability of the refined model is tested, and evaluation metrics include accuracy, sensitivity, specificity, precision, recall, F1-score, and mean squared error.^{115,153} Considerations include interpretability, resources, and expertise.¹⁵⁴ Continuous refinement and ensemble methods, like random forests and gradient boosting, enhance performance.^{155,185,187}

Effective models identify biomarkers,¹⁵⁷ understand disorder mechanisms,¹⁵⁶ and provide personalized treatment recommendations.¹⁴¹ Translating insights into practice improves diagnosis, prognosis, and treatment.^{142,143,160} Collaboration between AI and neurology experts, leveraging advanced techniques and refining models, enhances patient outcomes.

TABLE 5. AI-driven Precision Neurological Care: Emerging Tasks and Tool Descriptions

Task	Emerging AI tools and descriptions
Acute triage	AI assesses severity, prioritizes needs, and matches the patient with specialists for timely care.
Initial monitoring and intervention	AI tracks vitals, detects subtle patterns, and uses CNNs and long short-term memory networks to identify critical changes. It monitors electroencephalograms for seizures and analyzes images with CNNs and generative adversarial networks for abnormalities. ^{150,158,166}
Stabilization and complication prevention	AI integrates data using ML (random forests, gradient boosting machines, Hidden Markov models) to predict life-threatening events, triggering early interventions against sepsis. ^{32,159,185,186}
Ventilation weaning	AI analyzes respiratory and neurological trends, using ML to determine optimal weaning time and suggesting a personalized protocol. ¹⁸⁷
Medication optimization	AI analyzes genetics and history to recommend effective, low-side-effect drugs. It accelerates drug development by analyzing large datasets.
Long-term care and rehabilitation	AI-powered exoskeletons and neural implants adapt to needs using reinforcement learning, enabling natural movement control. ¹⁸⁸
Healthcare and home coordination	AI optimizes team schedules, ensuring equitable distribution and minimizing conflicts. It manages data flow using ML, ensuring timely communication and care both in hospital and at home, with NLP and computer vision alerting caregivers to issues. ^{82,162}
Rehabilitation support	AI adapts rehab programs to progress. Virtual reality provides therapy, and large language models enhance interaction with devices. ^{163,189}
Research trials	NLP identifies suitable trials by analyzing history, genetics, and current health. ¹⁸⁷
Recreational and Emotional Support	AI plays chess and Go, using algorithms to provide challenging interaction. ¹⁹⁰ AI robots offer companionship, cognitive support, and assistance, using NLP, RL, and computer vision to enhance well-being (See part 2, "Chatbots, Social and Emotional Robots" section).
Personalized Care	AI continuously adapts care based on responses and feedback. ^{112,114,115}
Learning Health System	AI analyzes patient data to optimize hospital operations and care protocols. (see part 3, "AI and LHS" section.)

Summary of the tasks involved in managing a complex neurological care scenario and the specific AI tools and techniques applied to each task. From acute triage to long-term rehabilitation and personalized care, AI systems are used to enhance decision-making, optimize treatments, and improve patient outcomes. The tools include various ML algorithms, neural networks, and natural language processing, each tailored to specific aspects of patient care and coordination

Abbreviations: AI = artificial intelligence; CNN = convolutional neural networks; ML = machine learning; NLP = natural language processing.

TABLE 6. Emerging Applications of AI Techniques in the Neurological Sciences

Application Area	Example
Neurology	Neuroimaging for diagnosis (Alzheimer's disease, Parkinson's disease) ^{97,164}
	AI-based decision support ¹⁶⁵
	Electroencephalography data for seizure prediction ¹⁶⁶
	NLP for clinical notes ¹⁶⁷
	Generating synthetic MRI scans for training ¹⁶⁸
	Data augmentation ¹⁶⁹
Neurosurgery	Deep learning for surgical planning ¹⁷⁰
	AI-powered surgical navigation ¹⁷¹
	Cranial nerve segmentation, instrument tracking ¹⁷²
	Enhancing tumor segmentation models with synthetic data ¹²⁹
Psychiatry	NLP and ML for mental health ¹⁷³
	ML for neuroimaging, genetic biomarkers ^{174,187}
	AI and VR for exposure therapy ¹⁷⁵
	AI-based conversational agents ¹⁷⁶
Basic neuroscience	ML, deep learning for neural data analysis ¹⁷⁷
	AI for neural connectivity data ¹⁷⁸
	GANs for synthetic neural data ^{51,52}
	AI for neural morphology analysis ¹⁵⁷
	Modeling complex brain connectivity patterns ^{52,178,179}
	Data imputation ¹⁸⁰
	Simulating progression of neurodegenerative diseases ¹³²
	Real-time monitoring of patient status from EEG data ^{55,122,166}

Examples of AI/ML tools—like deep learning, GANs, VAEs, diffusion models, NLP, and VR—are being applied across different neuroscience fields. Tables include specific use cases and references to relevant studies, highlighting advances and potential benefits for diagnosis, treatment, and research.

Abbreviations: AI = artificial intelligence; GANs = generative adversarial networks; ML = machine learning; MRI = magnetic resonance imaging; NLP = natural language processing; VAEs = variational autoencoders; VR = virtual reality.

A Case Scenario for Transformative AI-Driven Precision Neurological Care

This case highlights the transformative potential of AI in acute and long-term care—right now and in the near future. A 45-year-old woman is admitted to the neurocritical care unit after a severe brain and spinal cord injury from a crash while her vehicle was in autopilot mode. AI plays a key role in triaging her to the appropriate caregivers. On arrival, AI-powered systems track her vital signs, respiratory mechanics, and neurological status in real-time, detecting subtle patterns that might elude clinicians.

AI continuously monitors her EEG for seizure activity, predicting seizures and enabling timely interventions. As her condition stabilizes, AI shifts focus to preventing complications, like sepsis and brain herniation. When she shows readiness for extubating, AI advises on the best course of action, including identifying optimal drugs by analyzing her genetic data, medical history, and current condition.

The patient survives with quadriplegia and epilepsy. AI-powered assistive technologies become critical for her long-term care and rehabilitation, with neural implants connected to an exoskeleton providing support. AI organizes her schedules with healthcare professionals.

On discharge, AI continues to monitor her health, tracking vital signs, respiratory function, and other indicators, remaining vigilant for complications. It also gathers health-related data from devices like cell phones and fitness trackers. Personalized rehab programs, driven by ML, adapt to her progress, whereas virtual reality platforms provide engaging therapy exercises. AI-powered mental health tools offer psychological support.

LLMs assist her in interacting with digital devices, enabling control of her environment, communication, and access to information. By analyzing her medical history, genetic profile, and current health, an NLP system identifies suitable clinical trials. AI also monitors the flow of people and information in the hospital, ensuring critical information reaches the right personnel.

In her home, AI systems continue monitoring her health and social interactions. For recreation, she and her caregivers play games like chess and Go with AI opponents. Social and emotional robots offer companionship, cognitive stimulation, and assistance with daily activities. The AI systems learn and adapt through ongoing interaction. In a learning health system (see part 3), AI uses data from multiple patients to improve hospital and clinic operations.

By enabling personalized, proactive, and adaptive care, AI improves outcomes and quality of life for patients with severe neurological conditions. Standardizing and integrating vast healthcare data to fuel AI models is a monumental task. Ensuring the explainability, safety, and fairness of AI in medical settings is a challenge (see part 2). The costs

and infrastructure requirements also pose barriers to adoption. As research progresses and real-world implementations expand, the partnership between humans and AI is poised to redefine neurological care (Tables 5, 6).

Explosion of AI in the Neurological Sciences

Kurzweil foresaw “*The Singularity Is Near*,” where humans merge with machines to become super-intelligent beings or, at least, more effective human-machine systems.¹⁸¹ This future is rapidly approaching thanks to advances in AI (Fig S7), materials science, and large-scale initiatives, like the National Institutes of Health (NIH) Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative,¹⁸² which are unraveling the brain’s architecture to advance brain prostheses and other innovations.

At NIH (National Institute of Neurological Disorders and Stroke, National Institute on Aging, National Institute of Mental Health, National Institute on Drug Abuse, BRAIN Initiative), AI analyzes neuroimaging data to identify new brain cell populations, circuits, connections, and functional patterns, offering insights into cognitive architecture, function, and consciousness. AI models accelerate drug discovery by simulating compound interactions in the brain.

BRAIN Initiative-funded projects are refining brain-recording techniques, studying speech motor circuits, and developing AI to decode brain activity patterns into computer-generated speech, holding promise for individuals with paralysis because of amyotrophic lateral sclerosis or spinal cord injury. AI algorithms analyze imaging (MRI, CT, PET), EEG, demographics, and biomarkers for disease signatures in disorders like Alzheimer’s disease, Parkinson’s disease, multiple sclerosis, and epilepsy, enabling earlier, more effective treatments with fewer side effects.

In neurosurgery, AI-powered robots enhance procedures, minimize tissue damage, and improve patient safety through real-time imaging analysis and simulations. In psychiatry, AI analyzes speech, facial expressions, and behavior for detecting mental health disorders early, and AI chatbots offer 24/7 support and therapy tools. Computer vision uses AI algorithms to automatically process and extract insights from images and videos, with powerful applications in neurology. AI-powered techniques are used for automated diagnosis, analysis of brain lesions and atrophy, and segmentation of brain structures.

AI is also advancing in counterfactual and abductive reasoning, potentially enhancing patient-centered care through fine-grained analyses, challenging traditional diagnostic criteria, illuminating brain-behavior-environment

interactions, and informing interventions responsive to patient values and contexts.¹⁸³

AI is vast and probing the technical details of specific AI algorithms can provide neurologists with a deeper understanding of their workings and mathematical foundations. Addressing the challenges of deploying AI systems in real-world clinical neurology settings, including data integration, interoperability, regulatory hurdles, and user acceptance, is a long campaign.

Integrating AI tools into clinical practice awaits evidence of their effectiveness and lessons learned from their implementation. Exploring the long-term implications of AI for neurology, including changes to training curricula, clinical workflows, and the skills required for future neurologists to work effectively with AI systems, is crucial for the field’s future. The AI landscape in neuroscience and healthcare is rapidly evolving, with new applications and research emerging continually. This is a transformative time for neurology and neuroscience.¹⁸⁴

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Author Contributions

M.R. contributed to the conception and design of the manuscript; M.R. and J.D. contributed to the interpretation of studies included in the manuscript; M.R. and J.D. contributed to drafting the text and preparing the figures.

Potential Conflicts of Interest

Nothing to report.

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